

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
9 October 2003 (09.10.2003)

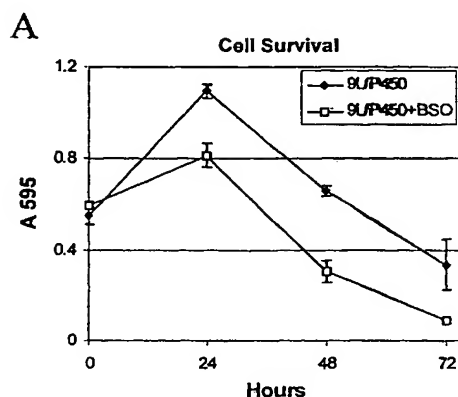
PCT

(10) International Publication Number  
**WO 03/083052 A2**

- (51) International Patent Classification<sup>7</sup>: C12N
- (21) International Application Number: PCT/US03/08743
- (22) International Filing Date: 25 March 2003 (25.03.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/367,311 25 March 2002 (25.03.2002) US
- (71) Applicant (for all designated States except US): THE TRUSTEES OF BOSTON UNIVERSITY [US/US]; 147 Bay State Road, Boston, MA 02215 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): WAXMAN, David, J. [US/US]; 30 Clements Road, Newton, MA 02458 (US). SCHWARTZ, Pamela, S. [US/US]; 7201 Seward Park Avenue S., Seattle, WA 98118 (US).
- (74) Agents: EISENSTEIN, Ronald, I. et al.; Nixon Peabody LLP, 101 Federal Street, Boston, MA 02110 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHOD OF USING ANTI-APOPTOTIC FACTORS IN GENE EXPRESSION



(57) Abstract: The present invention is directed to methods of prolonging the expression of a heterologous gene (transgene) in a cell, preferably a malignant cell. This method can be used to increase the concentration of a chemotherapeutic agent in a target cellular environment. Preferably, the present invention relates to methods of inhibiting apoptotic cell death to enhance transgene expression, such as gene-directed enzyme/prodrug therapy.

